

US Patent Application No. 10/663,506
Response and Amendment following Notice of Allowance

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims:

Claims 1 - 9 (Canceled).

Claim 10 (Previously presented): A rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid oral composition prepared by the process comprising:

- (a) dissolving rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid and from 0.001% to 3% (wt/wt) of an antioxidant in an alcohol;
- (b) dissolving PVP, a pH modifying agent, and a surfactant in water;
- (c) combining the aqueous and alcoholic solutions to provide a hydrocoholic solution;
- (d) adding the hydroalcoholic solution to a mixer containing one or more intragranular excipients;
- (e) granulating the mixture; and
- (f) drying the resulting granulation.

Claim 11 (Original): The composition of claim 10, wherein the pH modifying agent is selected from the group consisting of citric acid, sodium citrate, hydrochloric acid and mixtures thereof.

Claim 12 (Original): The composition of claim 11, wherein the alcohol is ethanol.

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Claim 13 (Original): The composition of claim 12, wherein the antioxidant is butylated hydroxyanisole and butylated hydroxytoluene.

Claim 14 (Original): The composition of claim 13, wherein the surfactant is sodium lauryl sulfate.

Claim 15 (Previously presented): A rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid oral formulation prepared by the process comprising:

- (a) dissolving rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid and from 0.001% to 3% (wt/wt) of an antioxidant in an alcohol;
- (b) dissolving PVP, a pH modifying agent, and a surfactant in water;
- (c) adding the aqueous and alcoholic solutions stepwise, and in one or more portions each, to a mixer containing one or more intragranular excipients;
- (d) granulating the mixture; and
- (e) drying the resulting granulation.

Claim 16 (Original): The composition of claim 15, wherein the pH modifying agent is selected from the group consisting of citric acid, sodium citrate, hydrochloric acid and mixtures thereof.

Claim 17 (Original): The composition of claim 16, wherein the alcohol is ethanol.

Claim 18 (Original): The composition of claim 17, wherein the antioxidant is butylated hydroxyanisole and butylated hydroxytoluene.

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Claim 19 (Original): The composition of claim 18, wherein the surfactant is sodium lauryl sulfate.

Claim 20 (Canceled).

Claim 21 (New): A solid pharmaceutical composition for oral administration comprising a granulation, said granulation comprising rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid,

a water soluble polymer in an amount of about 1 % to about 40% (wt/wt),

a surfactant in an amount of about 1 % to about 8% (wt/wt), an antioxidant from 0.001% to 3% (wt/wt), and a pH modifying agent.

Claim 22 (New): The composition of claim 21, wherein the water soluble polymer is PVP, hydroxypropylmethylcellulose, polyethylene glycol, or cyclodextrin or mixtures thereof.

Claim 23 (New): The composition of claim 22, wherein the water soluble polymer is PVP.

Claim 24 (New): The composition of claim 21, wherein the surfactant is polysorbate 80, sodium lauryl sulfate, sodium dodecyl sulfate, a salt of a bile acid, an ethoxylated vegetable oil, a polyoxyethylene-polyoxypropylene block copolymer, or a poloxamer.

Claim 25 (New): The composition of claim 24, wherein the surfactant is sodium lauryl sulfate or sodium dodecyl sulfate.

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Claim 26 (New): The pharmaceutical composition of claim 21, wherein the pH modifying agent is sodium citrate, citric acid, or dilute hydrochloric acid.

Claim 27 (New): The pharmaceutical composition according to claim 21, comprising rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid present in an amount of about 1% (wt/wt) to about 5% (wt/wt), polyvinylpyrrolidone in an amount of about 5% (wt/wt) to about 20% (wt/wt); a surfactant comprising sodium laurel sulfate in an amount of about 3% to about 5% (wt/wt), and citric acid.